

CLAIMS

What is claimed is:

1. A method of screening for an agent that alters adipose tissue development said method comprising:
 5 contacting a cell comprising a *Lpin1* gene with a test agent; and
 detecting a change in the expression or activity of a *Lpin1* gene product as compared to the expression or activity of a *Lpin1* gene product in a cell that is contacted with the test agent at a lower concentration, where a difference in the expression or activity of lipin in the contacted cell and the cell that is contacted with the lower
 10 concentration indicates that said agent alters adipose tissue development.
2. The method of claim 1, wherein said lower concentration is the absence of said test agent.
3. The method of claim 1, wherein the amount of *Lpin1* gene product is detected by detecting *Lpin1* mRNA in said sample.
- 15 4. The method of claim 3, wherein said level of *Lpin1* mRNA is measured by hybridizing said mRNA to a probe that specifically hybridizes to a *Lpin1* nucleic acid.
5. The method of claim 4, wherein said hybridizing is according to a method selected from the group consisting of a Northern blot, a Southern blot using DNA
 20 derived from the *Lpin1* RNA, an array hybridization, an affinity chromatography, and an in situ hybridization.
6. The method of claim 4, wherein said probe is a member of a plurality of probes that forms an array of probes.
7. The method of claim 3, wherein the level of *Lpin1* mRNA is
 25 measured using a nucleic acid amplification reaction.

8. The method of claim 1, wherein the amount of *Lpin1* gene product is detected by detecting the level of a lipin protein in said biological sample.

9. The method of claim 1, wherein said detecting is via a method selected from the group consisting of capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, and immunohistochemistry.

10. The method of claim 1, wherein said cell is cultured *ex vivo*.

11. The method of claim 1, wherein said test agent is contacted to an animal comprising a cell containing the *Lpin1* nucleic acid or the lipin protein.

12. A method of prescreening for an agent that alters adipose tissue development, said method comprising:

- i) contacting a *Lpin1* nucleic acid or a lipin protein with a test agent; and
- ii) detecting specific binding of said test agent to said lipin protein or nucleic acid.

13. The method of claim 12, further comprising recording test agents that specifically bind to said *Lpin1* nucleic acid or protein in a database of candidate agents that alter adipose tissue development.

14. The method of claim 12, wherein said test agent is not an antibody.

15. The method of claim 12, wherein said test agent is not a protein.

16. The method of claim 12, wherein said test agent is not a nucleic acid.

17. The method of claim 12, wherein said test agent is a small organic molecule.

18. The method of claim 12, wherein said detecting comprises detecting specific binding of said test agent to said *Lpin1* nucleic acid.

19. The method of claim 18, wherein said binding is detected using a method selected from the group consisting of a Northern blot, a Southern blot using DNA derived from a *Lpin1* RNA, an array hybridization, an affinity chromatography, and an in situ hybridization.

5 20. The method of claim 12, wherein said detecting comprises detecting specific binding of said test agent to said lipin protein.

21. The method of claim 20, wherein said detecting is via a method selected from the group consisting of capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, and immunohistochemistry.

10 22. The method of claim 12, wherein said test agent is contacted directly to the *Lpin1* nucleic acid or to the lipin protein.

23. The method of claim 12, wherein said test agent is contacted to a cell containing the *Lpin1* nucleic acid or the lipin protein.

24. The method of claim 23, wherein said cell is cultured *ex vivo*.

15 25. The method of claim 12, wherein said test agent is contacted to an animal comprising a cell containing the *Lpin1* nucleic acid or the lipin protein.

26. An isolated nucleic acid comprising a nucleic acid selected from the group consisting of:

20 a nucleic acid encoding a polypeptide selected from the group consisting of human lipin 1A (SEQ ID NO:3), mouse lipin 1A (SEQ ID NO:4), and mouse lipin 1B (SEQ ID NO:5);

a nucleic acid that hybridizes to a nucleic acid selected from the group consisting of mouse *Lpin1* (SEQ ID NO:1), and human *LPIN1* (SEQ ID NO2) under stringent conditions;

25 a nucleic acid having the sequence of a nucleic acid selected from the group consisting of mouse *Lpin1* (SEQ ID NO:1), and human *LPIN1* (SEQ ID NO2);

a nucleic acid that hybridizes to a nucleic acid selected from the group consisting of mouse *Lpin1* (SEQ ID NO:1), and human *LPIN1* (SEQ ID NO2) under stringent conditions and that encodes an lipin polypeptide;

5 a nucleic acid having the sequence of a nucleic acid amplified using primer 1 (SEQ ID NO:6) and primer 2 (SEQ ID NO:7) using cDNA from mouse cells or tissues as a template; and

a nucleic acid having the sequence of a nucleic acid amplified using primer 3 (SEQ ID NO:8) and primer 4 (SEQ ID NO:9) using cDNA from human cells or tissues as a template.

10 27. The nucleic acid of claim 26, wherein said nucleic acid is at least 15 nucleotides in length.

28. The nucleic acid of claim 26, wherein said nucleic acid comprises a nucleic acid selected from the group consisting of mouse *Lpin1* (SEQ ID NO:1), and human *Lpin1* (SEQ ID NO2).

15 29. A polypeptide comprising a polypeptide encoded by a nucleic acid of claim 26.

30. An antibody that specifically binds a polypeptide of claim 29.

31. The antibody of claim 31, wherein said antibody is a single-chain antibody.

20 32. The antibody of claim 31, wherein said antibody is a polyclonal antibody.

33. An isolated lipin polypeptide comprising a polypeptide that comprises an NLIP domain and a CLIP domain.

25 34. The polypeptide of claim 33 wherein said NLIP domain comprises the consensus sequence of SEQ ID NO: 10.

35. The polypeptide of claim 33 wherein said NLIP domain comprises the consensus sequence of SEQ ID NO: 11.

36. A transgenic animal comprising a recombinantly modified *Lpin1/LPIN1* gene such that said recombinantly modified gene does not transcribe a functional lipin protein.

37. The transgenic animal of claim 36, wherein said animal is homozygous for said recombinantly modified *Lpin1/LPIN1* gene.

38. The transgenic animal of claim 36, wherein said animal is a murine.

39. The transgenic animal of claim 36, wherein said animal is a mouse.

40. The transgenic animal of claim 36, wherein said animal is chimeric for cells comprising said recombinantly modified *Lpin1/LPIN1* gene.

41. A method of identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes, or atherosclerosis said method comprising: obtaining a biological sample from said organism; and detecting a mutation in a *Lpin1/LPIN1* gene or gene product from said biological sample.

42. The method of claim 41, wherein said mutation is selected from the group consisting of an insertion, a deletion, a missense point mutation, and a nonsense point mutation.

43. The method of claim 41, wherein said detecting is by a method selected from the group consisting a Southern blot, a DNA amplification, comparative genomic hybridization, immunohistochemistry, and cytogenetics.

44. The method of claim 41, wherein said detecting comprises detecting a mutation in a polypeptide.

45. The method of claim 44, wherein said detecting comprises a method selected from the group consisting of capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, and immunohistochemistry.

46. A method of identifying a predilection to developing one or more symptoms of lipodystrophy, obesity, diabetes, or atherosclerosis said method comprising:
obtaining a biological sample from said organism; and

5 detecting a *LPIN1* gene product wherein a difference in the amount or activity of said *LPIN1* gene product from said organism as compared to the *LPIN1* gene product from a normal healthy organism indicates that said organism has or is susceptible to a lipodystrophic phenotype, obesity, diabetes, atherosclerosis and related pathologies.

47. The method of claim 46, wherein the amount of *LPIN1* gene product is detected by detecting *LPIN1* mRNA in said cell.

10 48. The method of claim 47, wherein said level of *LPIN1* mRNA is measured by hybridizing said mRNA to a probe that specifically hybridizes to a *LPIN1* nucleic acid.

49. The method of claim 48, wherein said hybridizing is according to a method selected from the group consisting of a Northern blot, a Southern blot using DNA derived from the *LPIN1* RNA, an array hybridization, an affinity chromatography, and an *in situ* hybridization.

50. The method of claim 48, wherein said probe is a member of a plurality of probes that forms an array of probes.

20 51. The method of claim 47, wherein said level of *LPIN1* mRNA is measured using a nucleic acid amplification reaction.

52. The method of claim 46, wherein the amount of *LPIN1* gene product is detected by detecting the level of a lipid protein in said biological sample.

25 53. The method of claim 52, wherein said detecting is via a method selected from the group consisting of capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, and immunohistochemistry.

54. A method of mitigating a symptom of lipodystrohy, obesity, diabetes, atherosclerosis or related pathology, said method comprising modulating the concentration and/or activity of a *LPIN1* gene product in a cell of an organism.

55. The method of claim 54, wherein said modulating the concentration or activity of *LPIN1* gene product comprises upregulating or repressing expression of a heterologous *LPIN1* nucleic acid.

56. The method of claim 55, wherein said modulating comprises
5 upregulating or repressing expression of an endogenous *LPIN1* gene.

57. The method of claim 55, wherein said modulating comprises transfecting said cell with a vector that expresses a lipin protein.

58. The method of claim 57, wherein said vector constitutively expresses a lipin protein.

10 59. The method of claim 57, wherein expression of a lipin protein by said vector is inducible.

60. The method of claim 57, wherein expression of a lipin protein by said vector is constitutive.

61. The method of claim 54, wherein said cell is an adipocyte.

15 62. A method of inhibiting fat accumulation in a mammal, said method comprising inhibiting lipin expression or activity.

63. The method of claim 62, said inhibiting comprising inhibiting via a method selected from the group consisting of contacting a lipin nucleic acid with a ribozyme that specifically cleaves said lipin nucleic acid, contacting a lipin nucleic acid
20 with a catalytic DNA that specifically cleaves said lipin nucleic acid, transfecting a cell comprising a lipin gene with a nucleic acid that inactivates the lipin gene by homologous recombination with the lipin gene, transfecting a cell comprising a with a nucleic acid encoding an intrabody that specifically binds a lipin polypeptide, and transfecting said cell with a lipin antisense molecule.

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